derived from a second, different complement regulating protein not including combinations consisting of complement receptor 1 and complement receptor 2, complement regulating protein analogs wherein the short consensus repeats are rearranged, and complement regulating protein analogs consisting of as few as three short consensus repeats, wherein the protein analog binds C3b, C4b or C3b and C4b.

8. (five times amended) An analog of a protein selected from the group consisting of complement receptor 1, complement receptor 2, decay accelerating factor, membrane cofactor protein, C4 binding protein, [and] factor H, and these [complement regulating] proteins wherein the carboxy terminus is removed to allow the protein to be secreted, wherein the protein analog contains amino acid substitutions in the short consensus repeats which correspond to amino acid substitutions in the short consensus repeats of complement receptor one (SEQ ID No: 13) selected from the group consisting of:

CR1-4 with its first 122 amino acids (SCR1-2) (Sequence ID Nos 1 and 3) replaced with CR1 amino acids 497-618 (SCR 8-9) (Sequence ID Nos. 2 and 4) and CR1-4(8,9) with deletion of 194-253; and substitution of amino acids 271-543 with: T-R-T-T-F-H-L-G-R-K-C-S-T-A-V-S-P-A-T-T-S-E-G-L-R-L-C-A-A-H-P-R-E-T-G-A-L-Q-P-P-H-V-K (Sequence ID No. 11), or structurally similar amino

acids selected from the group consisting of (I,L,V), (F/V), (K/R), (Q/N), (D/E), and (G/A).

9. (six times amended) An analog of a protein selected from the group consisting of complement receptor 1, complement receptor 2, decay accelerating factor, membrane cofactor protein, C4 binding protein, [and] factor H, and these [complement regulating] proteins wherein the carboxy terminus is removed to allow the protein to be secreted, wherein the protein analog contains amino acid substitutions in the short consensus repeats which correspond to amino acid substitutions in the short consensus repeats of complement receptor one (SEQ ID No: 13 selected from the group consisting of:
79: D (amino acid 19 of Sequence ID No. 4); 37,79: Y,D (amino acid 37 of Sequence ID No. 2 and amino acid 19 of Sequence ID No. 4); 92: T (amino acid 32 of Sequence ID No. 4); 92-94: K...Y (amino acids 32-34 of Sequence ID NO. 3); 99,103,106: S...T...I (amino acids 39, 43 and 46 of Sequence ID No. 3); 109-112: D-T-V-I (amino acids 49-52 of Sequence ID No. 3); 110: T (amino acid 50 of Sequence ID No. 3); 111: V (amino acid 51 of Sequence ID No. 3); 112: I (amino acid 52 of Sequence ID No. 3); 1,3: Q...N (amino acids 1, 3 of Sequence ID No. 1); 6-9: E-W-L-P (amino acids 6-9 of Sequence ID No. 1); 12-16, 18-21: K-L-K-T-Q...N-A-S-D (amino acids 12-21 of Sequence ID No. 2); 27,29: S...K (amino acids 27,29 of Sequence ID No. 2); 37: S (amino acid 37 of

Sequence ID No. 1); 44, 47, 49: I...K...S (amino acids 44, 47, 49 of Sequence ID No. 1); 52-54, 57, 59: T-G-A...R...R (amino acids 52-54, 57, 59 of Sequence ID No. 1); 78-79, 82: K-G...F (amino acids 18-19, 22 of Sequence ID No. 3); 85, 87: Q...K (amino acids 25, 27 of Sequence ID No. 3); 12-16, 18-21: R-P-T-N-L...D-E-F-E (amino acids 12-21 of Sequence ID No. 1); 27,29: Y...N (amino acids 27, 29 of Sequence ID No. 1); 35, 64-65, 94: G...R-N...Y (amino acid 35 of Sequence ID No. 1, amino acids 4-5, 34 of Sequence ID No. 3), substitutions with structurally similar amino acids <u>selected from the group consisting of (I,L,V), (F/V), (K/R), (Q/N), (D/E), and (G/A),</u> and combinations thereof.

10. (four times amended) An analog of decay accelerating factor wherein one or more substitutions are introduced into the region of the protein corresponding to decay accelerating factor short consensus repeats SCRs 2-3 as shown in Sequence ID No. 17 selected from the group consisting of 180-187: S-T-K-P-P-I-C-Q (amino acids 54-61 of Sequence ID No. 4); 175-178: N-A-A-H (amino acids 49-52 of Sequence ID No. 4); 175-187: S-T-K-P-P-I-C-Q-N-A-A-H (Sequence ID No. 9); 130: R (amino acid 4 of Sequence ID No. 3); 145: D (amino acid 19 of Sequence ID No. 4); 77-84: K-L-K-T-Q-T-N-A-S-D (amino acids 12-21 of Sequence ID No. 2); 90-92: S-L-K (amino acids 27-29 of Sequence ID No. 2), substitutions with structurally similar amino acids <u>selected from</u>

F2 Cont

the group consisting of (I,L,V), (F/V), (K/R), (Q/N), (D/E), and (G/A), and combinations thereof.

F3

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~~13~~. (twice amended) The analog of claim 1 wherein the protein analog includes SCRs 2, 3 and 4 of DAF and has C3b cofactor activity, C4b cofactor activity and decay accelerating activity.

F4

13 ~~16~~. (four times amended) A method for making an analog of a protein selected from the group consisting of complement receptor 1, complement receptor 2, decay accelerating factor, membrane cofactor protein, C4 binding protein, [and] factor H, and these complement regulating proteins wherein the carboxy terminus is removed to allow the protein to be secreted, comprising

constructing a DNA sequence encoding a protein analog selected from the group consisting of complement regulating protein analogs containing short consensus repeats derived from a second, different complement regulating protein not including combinations consisting of complement receptor 1 and complement receptor 2, complement regulating protein analogs wherein the short consensus repeats are rearranged, and complement regulating protein analogs consisting of as few as three short consensus repeats, wherein the protein analog binds C3b, C4b, or C3b and C4b, and

expressing the DNA sequence in a suitable host for expression of the protein analog.

14 ~~18~~. (amended) The method of claim 16 wherein the protein used to form the analog is complement receptor one.

23. (five times amended) A method for making an analog of a protein selected from the group consisting of complement receptor 1, complement receptor 2, decay accelerating factor, membrane cofactor protein, C4 binding protein, [and] factor H, and these [complement regulating] proteins wherein the carboxy terminus is removed to allow the protein to be secreted, wherein the protein analog contains amino acid substitutions in the short consensus repeats which correspond to amino acid substitutions in the short consensus repeats of complement receptor one (SEQ ID No: 13) selected from the group consisting of:

CR1-4 with its first 122 amino acids (SCR1-2) (Sequence ID Nos. 1 and 3) replaced with CR1 amino acids 497-618 (SCR 8-9) (Sequence ID Nos. 2 and 4) and CR1-4(8,9) with deletion of 194-253; substitution of amino acids 271-543 with: T-R-T-T-F-H-L-G-R-K-C-S-T-A-V-S-P-A-T-T-S-E-G-L-R-L-C-A-A-H-P-R-E-T-G-A-L-Q-P-P-H-V-K (Sequence ID No. 11), or structurally similar amino acids selected from the group consisting of (I,L,V), (F/V), (K/R), (Q/N), (D/E), and (G/A),

the method comprising expressing a DNA encoding the protein analog in a suitable host cell and recovering the protein analog.

24. (five times amended) A method for making an analog of a protein selected from the group consisting of complement receptor 1, complement receptor 2, decay accelerating factor, membrane cofactor protein, C4 binding protein, [and] factor H, and these [complement regulating] proteins wherein the carboxy terminus is removed to allow the protein to be secreted, wherein the protein analog contains amino acid substitutions in the short consensus repeats which correspond to amino acid substitutions in the short consensus repeats of complement receptor one (SEQ ID No: 13) selected from the group consisting of:

79: D (amino acid 19 of Sequence ID No. 4); 37,79: Y,D (amino acid 37 of Sequence ID No. 2 and amino acid 19 of Sequence ID No. 4); 92: T (amino acid 32 of Sequence ID No. 4); 92-94: K...Y (amino acids 32-34 of Sequence ID NO. 3); 99,103,106: S...T...I (amino acids 39, 43 and 46 of Sequence ID No. 3); 109-112: D-T-V-I (amino acids 49-52 of Sequence ID No. 3); 110: T (amino acid 50 of Sequence ID No. 3); 111: V (amino acid 51 of Sequence ID No. 3); 112: I (amino acid 52 of Sequence ID No. 3); 1,3: Q...N (amino acids 1, 3 of Sequence ID No. 1); 6-9: E-W-L-P (amino acids 6-9 of Sequence ID No. 1); 12-16, 18-21: K-L-K-T-Q...N-A-S-

D (amino acids 12-21 of Sequence ID No. 2); 27,29: S...K (amino acids 27,29 of Sequence ID No. 2); 37: S (amino acid 37 of Sequence ID No. 1); 44, 47, 49: I...K...S (amino acids 44, 47, 49 of Sequence ID No. 1); 52-54, 57, 59: T-G-A...R...R (amino acids 52-54, 57, 59 of Sequence ID No. 1); 78-79, 82: K-G...F (amino acids 18-19, 22 of Sequence ID No. 3); 85, 87: Q...K (amino acids 25, 27 of Sequence ID No. 3); 12-16, 18-21: R-P-T-N-L...D-E-F-E (amino acids 12-21 of Sequence ID No. 1); 27,29: Y...N (amino acids 27, 29 of Sequence ID No. 1); 35, 64-65, 94: G...R-N...Y (amino acid 35 of Sequence ID No. 1, amino acids 4-5, 34 of Sequence ID No. 3), substitutions with structurally similar amino acids selected from the group consisting of (I,L,V), (F/V), (K/R), (Q/N), (D/E), and (G/A), and combinations thereof,

the method comprising expressing a DNA encoding the protein analog in a suitable host cell and recovering the protein analog.

25. (four times amended) A method for making an analog of decay accelerating factor wherein one or more substitutions are introduced into the region of the protein corresponding to decay accelerating factor short consensus repeats SCRs 2-3 as shown in Sequence ID No. 17 selected from the group consisting of

180-187: S-T-K-P-P-I-C-Q (amino acids 54-61 of Sequence ID No. 4); 175-178: N-A-A-H (amino acids 49-52 of Sequence ID No. 4);

175-187: S-T-K-P-P-I-C-Q-N-A-A-H (Sequence ID No. 9); 130: R (amino acid 4 of Sequence ID No. 3); 145: D (amino acid 19 of Sequence ID No. 4); 77-84: K-L-K-T-Q-T-N-A-S-D (amino acids 12-21 of Sequence ID No. 2); 90-92: S-L-K (amino acids 27-29 of Sequence ID No. 2), substitutions with structurally similar amino acids selected from the group consisting of (I,L,V), (F/V), (K/R), (Q/N), (D/E), and (G/A), and combinations thereof.

27. (twice amended) The method of claim 16 comprising expressing a DNA encoding a protein selected from the group consisting of complement receptor 1, complement receptor 2, decay accelerating factor, membrane cofactor protein, C4 binding protein and factor H, including in phase a DNA encoding [inserting into the protein analog] at least one short consensus repeat derived from a different protein selected from the group consisting of complement receptor 1, complement receptor 2, decay accelerating factor, membrane cofactor protein, C4 binding protein, and factor H, not including combinations consisting of complement receptor 1 and complement receptor 2.

28. (twice amended) The method of claim 16 wherein the protein analog includes SCRs 2, 3 and 4 of DAF and has C3b cofactor activity, C4b cofactor activity and decay accelerating activity.

30. (amended) The method of claim 16 further comprising isolated the analog and mixing with the isolated

analog a pharmaceutically acceptable carrier for administration to a patient in need thereof.

32. (twice amended) The DNA sequence of claim 31 inserted into an expression vector operably linked to control sequences compatible with a [compatible] host cell, which is capable, when transformed into the [host cell] expression vector, of expressing a DNA encoding the analog of claim 1.

~~34~~ 33. (three amended) A method for enhancing the C4b or C3b cofactor activity of a complement regulatory protein, wherein the protein has either C3b or C4b cofactor activity, comprising adding sequences to the protein conferring binding of the other ligand, either C4b or C3b, wherein the sequences are present in a protein selected from the group of naturally occurring complement receptor 1, complement receptor 2, decay accelerating factor, membrane cofactor protein, C4 binding protein, and factor H, not including combinations consisting of complement receptor 1 and complement receptor 2.

Remarks

Rejections under 37 C.F.R. §112

Claims 13 and 28 were rejected under 35 U.S.C. §112 as non-enabled for making a chimeric protein with DAF activity. Claims 1, 8, 9, 13, 16, 18, 23, 24, 27, 28, 30 and 32 were rejected under §112 as indefinite. These rejections are respectfully traversed.